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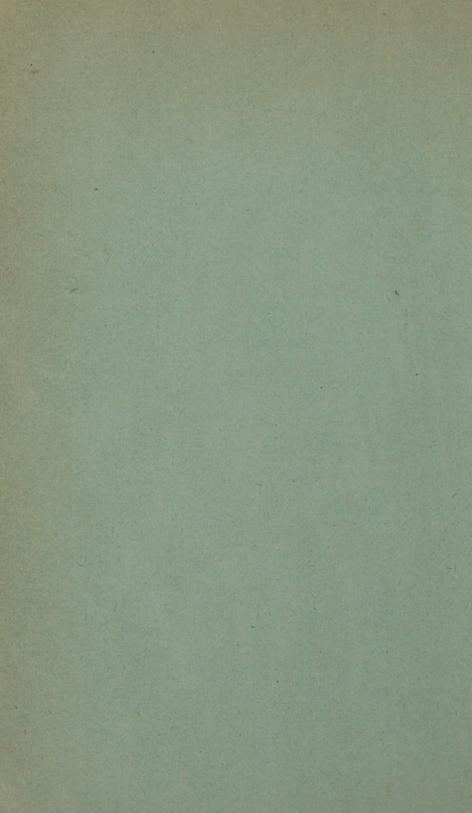
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(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

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ALTHOUGH this case has been published elsewhere in abstract,[1] I wish to record it now in full, as it is not only the first reported case of endocardial lesion due to the bacillus diphtheriæ, but it is the first time that this organism has been found associated with lesions of any of the internal organs other than the lungs; and for these reasons it must be regarded as a unique case.

The case occurred at St. Joseph's Hospital, Baltimore, in the service of my colleague, Dr. Frank A. Warner, by whose courtesy I am enabled to report it.

Constantine B., a Russian Pole, laborer, aged thirty-four years, married, was admitted to the hospital November 7, 1892, complaining of weakness, headache, and diarrhœa.

Family history. His father is living and healthy. His mother died with some disease of the eye. He knew nothing of his grandparents. One brother and one sister died in childhood; cause unknown. One son died in infancy. The patient denied having had any previous disease, and said that he had always been strong and healthy. His present disease began on November 1, 1892, when he was taken ill with severe chills, high fever, nausea and vomiting, diarrhœa, and with pains in the head, limbs, and abdomen.

On admission, at 6 P.M., November 7th, his temperature was 100.5°, his pulse 84 per minute, and his respirations accelerated. The eyes appeared normal. The skin was hot and dry. There were no wounds, spots, or hemorrhages in the skin anywhere. The lips and mucous membranes were pale. The tongue was dry, its edges red, its dorsum coated with a yellowish-brown fur. The mucous membrane of the mouth and pharynx appeared normal. The examination of the lungs was negative. The apex-beat of the heart was in the fifth intercostal space just within the nipple-line. The cardiac dulness began at the upper border of the fourth rib, the left sternal border, and extended to the apex. Both sounds were clear at apex and base. The second sound at the pulmonary cartilage was accentuated. The liver dulness extended from the upper border of the seventh rib to the costal margin in the

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[1] Studies in Diphtheria. The Johns Hopkins Hospital Bulletin, April, 1893, No. 30.

mammary line. The splenic dulness was obscure, the spleen was not palpable. The abdomen was resonant throughout. There was no gurgling or tenderness in the right iliac fossa The urine was negative.

A note made on November 18th showed that his state remained very much the same; but there was now some tympanites and some gurgling in the right iliac fossa. The tongue was dry and red. The temperature had been ranging about 102° in the evenings, the pulse was 84 and of fair volume. Examination of the heart and lungs was negative.

On November 21st he was worse, his pulse was 120 and of poor volume. Heart and lungs negative.

November 24. The patient has lost ground steadily the last three days. His temperature was subnormal and his pulse 150° and very weak. Albumin was found in his urine to-day. He died during the night of the 24th.

The *autopsy* was made by me eight hours after death.

Anatomical diagnosis. Acute ulcerative endocarditis with extensive thrombus formation of the superior surface of the mitral valve. Slight vegetative endocarditis of the aortic valve. Congestion and œdema of the lungs. Acute and chronic nephritis. Acute splenic tumor. Embolism ot the splenic and renal arteries; infarction of the spleen and kidneys. Acute parenchymatous degeneration of the liver, kidneys, and heart. Septicæmia.

Body 170 cm. long, well built; not emaciated. There are no œdema and no ecchymoses or other discoloration of the skin. The skin is pale. The pupils are dilated.

The brain and cord not examined. The subcutaneous fat is well developed. There is no œdema of the abdominal or chest walls. The muscles are pale.

In each pleural cavity there are a few cubic centimetres of clear serum. The pleural surfaces are smooth and free from adhesions. Both lungs are crepitant throughout. They are congested, especially at the bases and posterior portions of the lower lobes. The mucous membrane of the bronchi is red and somewhat swollen. Both lungs and the bronchial glands are deeply pigmented. On careful examination small ecchymoses are seen on the pleural surfaces.

The pericardium contains about fifty cubic centimetres of clear serum. Both layers are smooth and present small points of ecchymosis, which are best marked over the epicardium of the left auricle.

The left ventricle is rather strongly contracted. The heart is larger than normal and weighs 350 grammes. The myocardium is of a pale-red color and is less firm than normal. All the cardiac cavities contain dark fluid blood and yellowish-white clots. On opening the left auricle there is seen to project through the auriculo-ventricular orifice a granular-looking and in some places mottled gray and red thrombus mass, which completely closes the orifice. This mass is everywhere intimately adherent to the superior or auricular surface of the mitral valve. On opening the ventricle the whole area of this surface of the valve is seen to be covered with this intimately adherent and generally grayish white thrombus mass, which presents in places a few granulations. This mass varies in thickness from 2 mm. to 1 cm. On incision it is found to be thickest about the middle of the valve. At many points it becomes thinner along the free margins of the valve, and is then often continued down on the chordæ tendinæ. At the base of the valve toward the

auriculo-ventricular ring on the superior surface the endocardium at the margin of this thrombus mass is curled up, leaving a red, roughened surface of ulceration. The thrombus is thickest over the anterior segment, and from here it sends down a teat-like projection, 5 mm. in diameter at its base, into the cavity of the ventricle. The two segments of the valve are bound together by the thrombus mass, which on incision is tough and dense and of a grayish-white appearance. At the point of juncture between the thrombus and the ulcerated valve the tissue is red and injected.

The inferior or ventricular surface of the valve presents a few small granular elevations, which on removal leave a red ulcerated surface. Otherwise this aspect of the valve is normal.

When the surfaces of the thrombus are brought together by closure the mass measures 17 mm. in diameter. At least half the diameter of the orifice is obstructed by the thrombus.

Along the ventricular aspect of the aortic valve, just below the level of the corpora Arantii, there is a narrow row of exquisite, minute fresh vegetations of a light-red color. The rest of the valve is unchanged and there are no uncovered points of ulceration.

In the meshes of the columnæ carnæ of the left auricle and ventricle there are soft grayish-white non adherent coagula. The parietal endocardium elsewhere is normal and presents no ulcerations.

The right auricle and ventricle contain dark fluid blood and non-adherent coagula. The valves and the walls are normal. The auricular appendages contain non-adherent clots, but no thrombi.

There is slight hypertrophy of the left ventricle. The circumference of the mitral valve is 9.5 cm. ; of the tricuspid, 11 cm. ; of the aortic, 7 cm. The coronary arteries are normal, as are the aorta and the pulmonary artery.

The liver is large, and projects below the costal margin in the mammary line. The edges are round, the surface smooth. On section the surface is pale and opaque. The lobules are visible. There is no apparent connective tissue increase, and no areas of necrosis. The consistence is normal. In the gall-bladder there is a small amount of bile, of a syrupy consistence. The gall-bladder and the bile-duct are normal. The spleen is large, weighing 400 grammes and measuring 15 x 10 x 4.5 cm. The surface in general is smooth, with here and there small scattered pale gray points in the capsule. The notch is well marked. On section the organ is of a dark red color, in general, with here and there lighter areas. The organ is soft, but not diffluent, and throughout nearly its whole extent is the seat of infarction. The trabeculæ are visible, the Malpighian bodies not. In the larger branches of the splenic artery there are white and red thrombus masses, which are often intimately adherent to the vessel wall.

The kidneys are of about the same size and general appearance. They are smaller than normal, and together weigh 320 grammes. The capsules are readily removed. The main trunk of the renal artery of each side is normal; but in both kidneys in many of the branches of medium size there are grayish-white embolic masses which completely plug the lumen. Some of these masses can be pressed out, others are firmly adherent to the vessel walls. Beneath the surface of both kidneys, scattered everywhere, there are points of ecchymosis. At the middle of the convexity of each organ there is a large, raised yellowish-

gray area, with dark red margins. These areas extend over a large surface, and the one in the left kidney involves fully one-sixth of the organ. On section of the kidneys these areas are seen to be irregularly triangular in outline. They are of a yellowish-gray color, and are firmer than the rest of the kidney tissue. These extensive infarcts involve both medullary and cortical tissue. Scattered over the surface and through the organs there are numerous smaller white infarctions, which, like the large ones, are surrounded by a dark hemorrhagic zone. These hemorrhagic zones are especially well marked just beneath the surface of the organs.

At one place the infarcted area is extensively softened, and is bordered by a deep hemorrhagic zone, giving somewhat the appearance of a recent corpus luteum. The cortex of both kidneys, where not involved in infarctions, is swollen, pale, and opaque. The striæ are indistinct, the glomeruli appear congested. The medullary portions of the kidneys are congested.

The pelves, ureters, and bladder are normal.

The pancreas, adrenal bodies, and testes are normal.

The mucous membrane of the stomach is injected. The duodenum and the jejunum are pale. In the ileum and in the upper part of the large intestine the solitary follicles are swollen and congested, but present no sign of ulceration. The Peyer's patches just above the ileo-cœcal valve are swollen and red.

The mesenteric glands are not specially enlarged.

The pharynx, tonsils, and the mucous membrane of the larynx and trachea present no pathological changes. The nasal fossæ and the vault of the pharynx were not examined.

Fresh frozen sections of the heart, liver, spleen, and kidneys were studied, but as the various histological changes found showed very much better in hardened sections, a description of the microscopical appearances of the fresh tissues is omitted.

Cover-slip preparations made at the time of the autopsy from the mitral valve, the spleen, and the kidneys, showed in great numbers and in pure cultures a bacillus of the size and morphological appearances of the bacillus diphtheriæ. Cultures were made at once, with the usual precautions, on plain agar-agar from the ulcerated surface of the mitral valve, and from the lungs, spleen and kidneys. After twenty-four hours in the thermostat there were numerous small isolated colonies in each tube. Cover-slip preparations from a number of these colonies showed always the same organism, which had the same appearance as those seen in the cover-slip preparations from the fresh organs.

The bacillus was non-motile. It varied in shape and size. It occurred both on coverslip preparations made from cultures and in sections from the mitral valve and the kidneys, usually as a straight rod with rounded ends, but it often assumed irregular and bizarre shapes. In some one or both ends were swollen; in others, portions of the bacilli stained more deeply than others, giving a beaded appearance to the organisms.

The bacillus from cultures and in the tissues stained well and clearly with Gram's method and with Weigert's fibrin stain.

On glycerin agar-plates, after remaining twenty-four hours in the thermostat, the colonies were round or oval, elevated and coarsely granular, with ill-defined borders. The superficial colonies were large, very coarsely granular, and irregular in outline. With the naked eye

the colonies were grayish-white in color. On slanting glycerin agar and plain nutrient agar the growth was abundant, and made up of small well-defined grayish-white colonies. The bacillus grew well on gelatin.

In alkaline bouillon the growth occurred as small, irregular, grayish-white specks at the bottom and along the sides of the tube. The bacillus grew well on steamed potato, and could be cultivated for generations on this medium. The growth was, however, always invisible. There was a rapid and luxurious growth on blood-serum.

The organism was cultivated on a variety of media side by side with cultures of the bacillus diphtheriæ obtained from undoubted cases of primary faucial diphtheria, and was always found to be identical in both its morphological and cultural properties with that organism.

After repeated experiments this bacillus has failed to kill guinea-pigs and rabbits.

Portions of the mitral valve, of the left ventricle, of the lungs, liver, spleen, and kidneys, and other organs were hardened in alcohol. Sections of these were stained with hæmatoxylin and eosine, methylene-blue and eosine, and with Weigert's fibrin stain, and studied.

Heart. For histological study sections were made at several places perpendicularly through the mitral valve and the superimposed thrombus mass. These sections included, in addition to the thrombus and the whole extent of the valve, corresponding portions of the endocardium and the musculature of the left auricle and ventricle. The starting-point of the process on the valve could be best studied near the base of the valve, just below the auriculo-ventricular ring, for here it is more recent, and its various steps can be accurately traced. The lesion is somewhat irregular in extent, extending higher up toward the base of the valve in sections made from some places than in those made from others. In sections made through the posterior segment the change in the valvular tissue extends almost to the base of the valve, and in sections made from the anterior segment not quite so far. In these sections beginning near the base of the valve there are various changes to be noted in the endothelial cells of the endocardium. In many of them the nucleus stains poorly, and the surrounding protoplasm is swollen and granular; others have lost their nuclei; many of the cells are desquamated. In some of the cells bacilli can be made out. These are more numerous in the desquamated cells. At this point there are no changes to be noted in the underlying tissue of the endocardium. Farther down, and beginning just above the thrombus mass, there is a large area very rich in cells, which extends through the entire thickness of the endocardium. Here the endothelial cells are entirely lost, only a few swollen, granular-looking, desquamated ones being made out. At this point there is seen in all the sections examined a considerable local reaction, shown by a great increase in the number of cells. These cells are for the most part poly-nuclear leucocytes, but there are a considerable number of round cells of about the size and appearance of large mononuclear leucocytes, and some more or less spindle-shaped cells. This cell-infiltration here involves the whole thickness of the endocardium proper, and in some sections the underlying muscle tissue as well.

The cells are more numerous toward the free border, where the poly-morphous nuclear variety predominate, and they gradually lessen in number toward the muscle-tissue and toward the base of the valve. Along the free edge and extending to some depth, there is a well-marked

nuclear fragmentation. Some of the cells have lost their nuclei, and the latter lie free in the tissue. These fragments may appear as round, highly refractive, intensely staining dots, or may assume very irregular and bizarre shapes. In places the tissue in which the cells lie is hyaline, staining diffusely with eosine, and showing characteristic threads of fibrin with Weigert's fibrin stain.

Both at the margin of this area, and extending a considerable distance into the tisue, bacilli can be made out. The bacilli lie both inside the cells and free in the tissue. This area is covered by a pseudo-membrane, that is continuous with that covering the rest of the valve and forming the thrombus mass. At this point the pseudo membrane is composed of a dense mass of fibrin laid down in succesive layers, and staining diffusively with eosine, and characteristically with Weigert's fibrin stain. In between the meshes of the fibrin layers there are numerous cells, both large mononuclear cells and polymorphous-nuclear leucocytes, the latter variety predominating. Many of the cells contain bacilli in numbers. In the fibrin meshes there are also parts of disintegrated cells, free nuclei and fragmented nuclei. These latter often assume bizarre shapes, and they stain intensely with aqueous fuchsine and alkaline methylene-blue. Numerous bacilli appear in scattered clumps and in large zoöglea masses.

Below the area of cellular infiltration described in the endocardium, this membrane throughout its whole extent on the upper surface of the valve is hyaline, and stains diffusely with eosine, and very few nuclei can be made out. The endothelial cells on the free surface are entirely lost, and between this hyaline material and the thick thrombus mass there is an irregular, thick line, staining deeply with the aniline dyes, and which is made up of myriads of bacilli. As the free or unattached end of the valve is approached, in addition to the endocardial tissue, the underlying muscle tissue of the valve to a considerable depth is hyaline, and contains no well-preserved nuclei. There are some fragmented nuclei to be seen. This hyaline material stains diffusely and characteristically with eosine and with picric acid. At the edge of the valve, in sections made from various places, this hyaline tissue is covered with a mass of fibrin laid down in successive layers, and containing in its meshes numerous cells and bacilli. The cells here are in various stages of degeneration; many are swollen and granular, and contain bacilli. There is an intense nuclear fragmentation, and many free nuclei are seen. These cells are for the most part polymorphous nuclear leucocytes. At the margin of the free end of the valve, under this pseudo-membranous formation, there is a considerable local reaction, which is in many respects similar to the area described near the base of the valve. The chief point of difference is that here there seems to be a complete necrosis of the tissue of the part. The outlines of the cells are lost, the nuclei stain poorly, and there is an exquisite nuclear fragmentation, the fragments often taking bizarre shapes. The tissue stains diffusely with eosine and picric acid. The thrombus mass, which covers the whole of the upper or auricular surface of the valve, is composed of this fibrin formation containing cells, and of a diffusely staining mass of fibrin containing myriads of bacilli. These latter form a deep and irregular line along the free surface of the thrombus. Everywhere in the fibrinous material they are diffusely scattered in irregular clumps and in large zoöglea masses. In sections stained with eosine and methylene-blue or hæmatoxylin, the hyaline fibrinous material stains homogeneously, and the bacilli take up the

nuclear dye intensely. With Weigert's fibrin stain the hyaline material is seen to be made up of threads and bands of fibrin, and the bacilli stain deeply. In the outer portions of the thrombus but few cells are seen, and these are of the polymorphous-nuclear type only.

In all the sections studied the muscle cells of the musculature of that portion of the auricle included in the sections are normal. There is a slight fibrous myocarditis.

The muscle tissue of the valve itself presents a striking change. That portion of the muscle tissue just beneath the necrotic endocardium, toward the outer or free edge of the valve, is in all the sections studded hyaline, and stains diffusely. In several places there are small collections of red blood-corpuscles that still preserve their form.

In sections from one place there is on the under or ventricular surface of the valve near its free edge an area of cell infiltration, with loss of the endothelial cells and with nuclear fragmentation. There is a pseudo-membranous formation on the surface here. The process at this point is recent, and is similar to that seen on the upper surface near the base of the valve. At several places midway in the thickness of the valve there are focal areas of necrosis of the muscle-cells, with nuclear fragmentation. About these areas there are polymorphous-nuclear leucocytes in various stages of degeneration. No bacilli are made out in these areas. In still other places there are areas of cellular infiltrations with proliferation of the fixed cells and the presence of polymorphous-nuclear leucocytes. Many of the cells are degenerated, and there is considerable nuclear fragmentation. In the centre of one of these areas, which can be traced through a number of sections, there is a bloodvessel filled with a large zoöglea mass of bacilli. There are few bloodvessels present in the sections examined, but those seen are large and evidently dilated.

The bacilli described in the process on the valve are in pure culture and are morphologically identical with those in cover-slip preparations made in the fresh state and with those grown in the cultures made at the autopsy.

Kidneys. Study of sections made from portions of the kidneys not involved in infarctions shows in some glomeruli thickening of the capsule of Bowman, with some desquamation of the capsular epithelium. The glomeruli show an increase of cells, and they nearly fill the capsules. In some very thin sections stained with eosine and methylene-blue the capillaries are seen to be distended with blood and to contain large numbers of polymorphous-nuclear leucocytes. Here and there a few bacilli can be made out inside the capillaries. There is no necrosis of cells to be made out in the glomeruli. The afferent vessels are distended with blood.

The intertubular connective tissue is increased in amount. The epithelial cells of the tubules are swollen and granular. The lumina of the convoluted tubules are in many places completely filled with these swollen and granular cells. In many tubules the epithelial cells are detached in large numbers from the basement membrane. The nuclei often stain badly and in some cells not at all. In some tubules scattered bacilli can be made out. There is no nuclear fragmentation. Scattered throughout the kidneys there are numerous areas of hemorrhage into the tubules. In these areas the tubules are distended with blood, and the epithelium is flattened out or completely lost, and inside some of the tubules so affected numerous bacilli are seen. These hemorrhagic areas are more

numerous in the cortex near the surface of the kidney. The vessels just under the capsule are distended, and here and there there is hemorrhage into the surrounding tissue.

Sections cut across a large branch of the left renal artery present a peculiar appearance. In the side of the vessel nearest the cortex and occupying about one-fourth of the lumen of the vessel there is a mass of red blood-cells containing large numbers of polymorphous nuclear leucocytes, which are for the most part massed in clumps containing both free and fragmented nuclei. In this area a few bacilli are seen. The rest of the lumen of the vessel is filled with a mass of hyaline material staining diffusely with eosine and showing characteristic fibrin threads with Weigert's stain. In this material there are enormous numbers of bacilli usually in large zoöglea masses. In the fibrin meshes there are many polymorphous-nuclear leucocytes, which are often massed together, and which show a well-marked nuclear fragmentation. These leucocytes are especially numerous and form a thick line at the junction of the line of red blood-cells with the fibrinous material. That portion of the vessel wall in relation with the mass of red blood-cells appears normal. The rest of the wall of the vessels presents an interesting picture. Here there are various changes met with in all three coats.

On one side, at a point where the fibrinous material joins the mass of red blood-cells and between the latter and the vessel wall, the endothelial cells of the intima are for the most part desquamated. Those remaining attached are swollen and granular. The desquamated cells lie in the fibrinous material, are swollen and granular, and many have lost their nuclei. Some contain bacilli, which often have a transverse, beaded appearance. Extending from this point all the way around the side of the vessel until the mass of red blood-cells is reached again, the endothelial cells are lost over large areas. In many places the fenestrated membrane of the intima is stripped off. Around the whole of the three-fourths of the circumference of the vessel where these changes in the intima are noted there are large numbers of polymorphous-nuclear leucocytes and bacilli imbedded in the fibrinous material already described. Just here there are many leucocytes and endothelial cells containing bacilli. Throughout this three-fourths of the circumference of the vessel the media is the seat of a peculiar change. Here, forming a line between the junction of the intima and media, there are a large number of cells. These are especially numerous in those places where the fenestrated membrane is lost.

The muscle-cells at these points have lost their nuclei and stain diffusely with eosine; there is also considerable nuclear fragmentation, but it is never so extensive as that seen outside the intima and in the mass of fibrin. The cells above described are for the most part polymorphous-nuclear leucocytes; but there are also many large, round cells with large single nuclei. Here and there in these areas of cellular infiltration bacilli can be made out, but they are never numerous. In some places the leucocytic invasion can be traced down along the muscle bands to the adventitia. At one point and over a considerable area the muscle-cells of the whole thickness of the media are hyaline, have lost their nuclei, and there is considerable nuclear fragmentation. Here there are a large number of leucocytes, and a few bacilli can be made out here and there. The adventitia shows a recent proliferation of the fixed cells,

and the tubules in the neighborhood are atrophied. Nowhere can one trace leucocytes entering the media from the adventitia.

Sections cut through a large infarction extending through the medulla and the cortex of the left kidney show many interesting changes. The cells of the kidney tissue in this area are entirely necrotic and stain deeply with eosine. Only here and there do the nuclei stain at all. In many places the tubules are filled with a hyaline material which stains diffusely with eosine. In sections stained with Weigert's fibrin stain these hyaline masses are seen to contain many fine threads of fibrin. A fibrinous network can also be made out between the tubules both in the intertubular tissue and inside of the small bloodvessels. These latter are distended and the nuclei of the cells of their walls do not stain. The cells of the glomeruli in this area are necrotic and their nuclei do not stain. The glomerular capillaries are often filled with threads of fibrin. All through the infarcted area there are great numbers of bacilli, which are seen in scattered clumps and in large zoöglea masses. These lie inside of the tubules, in the intertubular tissue inside the capillaries and small vessels. Many of the glomeruli contain large masses of bacilli; indeed, in some glomeruli nothing can be seen but a large zoöglea mass of bacilli.

In the centre of the infarcted area no leucocytes are seen. Along the border of the infarct there is a dense infiltration, with polymorphous-nuclear leucocytes, with a great deal of nuclear fragmentation. In some places this leucocytic infiltration can be traced for some distance into the infarcted area. Here two appearances are met with. In some places about a dense mass of bacilli which lie in a glomerulus, in tubules, in capillaries, or, as often occurs, in the intertubular tissue, there is seen a dense infiltration, with polymorphous-nuclear leucocytes. Many of the nuclei of these cells lie free in the tissue, are fragmented, and show bizarre shapes. In most of these areas the tissue is hyaline and necrotic, and stains diffusely with eosine, and with Weigert's fibrin stain fine fibrin threads can be made out. In other places, extending for some distance into the infarcted area, the capillaries and small bloodvessels are distended, with large numbers of polymorphous-nuclear leucocytes.

The area of infarction does not extend quite to the free border of the cortex, for nearly everywhere just under the capsule the tissue cells stain well. The vessels here are distended with blood, and some of the capillaries can be traced running down into the infarcted area. The endothelial cells of the walls of these vessels stain well; their lumina contain red blood-corpuscles and great numbers of polymorphous-nuclear leucocytes. In places there is hemorrhage into the tubules and into the intertubular tissue. Often polymorphous-nuclear leucocytes, free nuclei, and nuclear fragments can be made out in the hyaline contents of the tubules and in the intertubular tissue at this border of the infarction. In most of the sections studied the line of the infarction is clear cut. In some sections the leucocytic invasion extends for some distance into the infarted area.

The bacilli seen in all the sections of the kidneys are invariably morphologically identical with those described on the heart-valve and obtained in the cultures. They are the only kind of bacteria present.

Liver. The liver cells are swollen and granular, but their nuclei stain well. In many places the cells are filled with bile pigment. The capilla-

ries are wider than normal, and contain red blood-cells and large numbers of polymorphous-nuclear leucocytes. The central veins of the lobules generally are distended; some are very much so. In some sections the lumina of the central veins, beside red blood-cells, contain many large cells of the size and appearance of liver-cells. The nuclei of these cells do not stain with the nuclear dyes, and the cell bodies stain diffusely with eosine. In these areas the liver cells around the central vein, to the depth of several rows, present the same characters. In these areas there is no nuclear fragmentation and no leucocytic infiltration. In one section there is an area near a central vein in which the nuclei of the liver-cells do not stain; the cell bodies here stain deeply with eosine. In this area there is no leucocytic invasion and no bacilli are seen.

A few scattered bacilli can be made out here and there in the liver capillaries. In some sections large zoöglea masses are seen. In sections stained with Weigert's fibrin stain no fibrin can be made out in the liver. There is some increase of connective tissue in the portal systems.

Spleen. In the infarcted areas of the spleen the tissue is filled with red blood-cells and polymorphous-nuclear leucocytes, accompanied by an extensive nuclear fragmentation. Tissue stains deeply with eosine, and in sections stained with Weigert's fibrin stain a great deal of fibrin is seen both in and outside of the capillaries. Bacilli are seen in great numbers, both in scattered clumps and in large zoöglea masses, both in the bloodvessels and free in the tissue. Scattered in the splenic pulp there are numerous peculiar crystalline masses. They are of an orange color, and have the appearance of a mass of thread-like lines radiating from a common centre.

Lungs. Microscopical examination of sections of the lungs shows nothing of special interest. There is a slight amount of chronic interstitial pneumonia, with deep pigmentation. In places, small hemorrhages into the pleura cannot be made out. The bloodvessels about these areas are dilated.

The epithelial cells of the bronchi are swollen, and in some places desquamated. No bacilli are seen in the capillaries or in the larger bloodvessels.

The bacillus found in such great numbers in this case has been carefully studied by Prof. Welch, by myself, and by several other workers in his laboratory, and none of us has been able to distinguish any difference between it and the bacillus diphtheriæ obtained from typical cases of primary faucial diphtheria, either morphologically or by cultural methods. It has invariably reacted typically to all the cultural and staining tests known.

Dr. A. C. Abbott, of the Laboratory of Hygiene of the University of Pennsylvania, has also failed to distinguish it by these methods from the ordinary bacillus diphtheriæ. Furthermore, he has found that the bacillus of my case shows the same reaction described by him as to change of form as does the ordinary bacillus diphtheriæ on changing it from blood-serum to glycerin agar-agar, and *vice versa.* Abbott[1] has found that the long, clubbed, irregularly staining individual bacilli

[1] Abbott: Journal of Pathology and Bacteriology, October, 1893.,

diphtheriæ seen in cultures made on blood-serum, when transferred to and grown on glycerin agar-agar are far less voluminous, much shorter, and many-shaped. The reverse he found to occur when bacilli previously grown on glycerin agar-agar were transferred to blood-serum.

The bacillus of this case, even when large doses were used, has not proved pathogenic for guinea-pigs or rabbits. Animals kept for months after inoculation are alive, and show no paralysis.

These facts bring up the interesting question of the existence of a true bacillus diphtheriæ pathogenic for human beings and not for animals.

Abbott,[1] in August, 1891, reported two cases of primary faucial diphtheria which bear upon this point. In the first case he obtained a bacillus, the only difference between which and the bacillus diphtheriæ was that it was not pathogenic for animals. The bacillus of the second case showed a more luxuriant growth than usual on various media and a visible growth on potato, and also failed to kill animals.

Abbott[2] has lately reported two cases of membranous rhinitis, in both of which the bacillus diphtheriæ was found. Cultures from one case killed guinea-pigs in forty-eight hours, and cultures from the second case failed to kill these animals.

The behavior of the bacillus found in my case goes to strengthen the argument that the intensity of the virulence of the bacillus diphtheriæ fluctuates.

The fact that the patient was affected twenty-four days before death occurred, and the absence of any mechanical interference to the circulation on account of the valvular lesion, together with the histological appearances of the process on the mitral valve, would seem to show that the organism concerned in the etiology of the affection was not possessed of a high degree of virulence. These facts, added to the state of the process in other organs, point rather to a gradual loss of resistance on the part of the individual, which finally allowed such a rapid multiplication of the bacilli on the heart valve as to produce a genuine septicæmia, and finally extensive infarctions in the spleen and kidneys. It is probable that the large area of renal territory comparatively suddenly thrown out of use as the result of the numerous and large infarctions, together with the acute nephritis present, was the immediate cause of death. The individual was able to resist the bacilli for some time, and it was only after this resistance was exhausted by a prolonged struggle that the bacilli and their products were capable of multiplying to cause septicæmia and embolic processes.

The length of time that the bacilli remained in the body may explain their lack of virulence for animals. The fact that the bacilli found in this case were not pathogenic for rabbits and guinea-pigs strengthens the

[1] Abbott: Johns Hopkins Hospital Bulletin, August, 1891.
[2] Abbott: Medical News, May 13, 1893, vol. lxii., No. 19.

position of those observers who hold that the lack of pathogenicity for animals in a bacillus otherwise identical with the bacillus diphtheriæ is not sufficient ground for classing it with the "pseudo-diphtheria bacillus."

It is well known that various bacteria obtained from a variety of lesions in the human being often fail to kill animals. I have several times found that large numbers of pneumococci obtained from the lungs of fatal cases of pneumonia have failed to kill, or even to produce local reaction in rabbits.

It is now generally recognized that bacteria when obtained from old lesions, as, for instance, pneumococci from the gray hepatization of pneumonia, frequently lack virulence for animals. What happens with the pneumococcus and other pathogenic bacteria in this regard may well obtain for the bacillus diphtheriæ.

While this is the first case in which the bacillus diphtheriæ has been obtained from lesions of internal organs other than the lungs, Frosch[1] has cultivated this organism from various internal organs in ten out of fifteen cases of ordinary diphtheria. Other observers have reported single cases in which they have gotten similar results.

Booker[2] has lately published a case of primary laryngeal diphtheria, in which he obtained pure cultures of the bacillus diphtheriæ from one of the submaxillary glands and from the spleen.

When the suggestion of Frosch, that comparatively large pieces of organs are to be used in making cultures in these cases, is generally adopted, it will probably be found that the bacillus diphtheriæ obtains entrance into the circulation, in fatal cases at least, with greater frequency than is commonly supposed.

The absence of any demonstrable infection atrium in my case leaves us in the dark as regards the mode in which infection took place.

Not until other cases of infection of internal organs by the bacillus diphtheriæ have been observed can the interesting question of the modification of the virulence of this organism when subjected to prolonged habitation in the human body and the action of the blood-serum be cleared up.

The examination of sections from the various organs affected shows that the lesions due to, and the reaction of the tissues to, the organism found are identical with those described by Oertel[3] for diphtheria in man, and by Welch and Flexner[4] for experimental diphtheria in animals.

It is interesting to note that the lesions found in the thrombosed renal artery were identical with those described on the mitral valve, though

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[1] Frosch: Zeit. f. Hygeine u. Infectionskrankheiten, 1893, Band xiii., pp. 49-52.

[2] W. D. Booker: Archives of Pediatrics, August, 1893, vol. x., No. 8.

[3] Oertel: Die Pathogenese der epidemischen Diphtheria. Nach ihrer histologischen begrundung. Mit Atlas. Vogel, Leipzig, 1887.

[4] Welch and Flexner: Johns Hopkins Hospital Bulletin, No. 15, August, 1891. Also ibid., No. 20, March, 1892.

evidently of more recent date.   The great number of bacilli seen in the infarcted areas in the kidneys cannot have been due solely to conveyance by emboli, but must have in large part depended upon a rapid multiplication of the organisms brought to the tissue with the embolic masses after the normal resistance of the tissues was destroyed by the necrosis resulting from the infarction.

The hemorrhage into that part of the kidneys not involved in infarctions is readily explained by the direct action of the bacilli and their products upon the cells of the vessel walls.   The destruction of renal tissue by the action of the bacilli and their toxines was extensive.
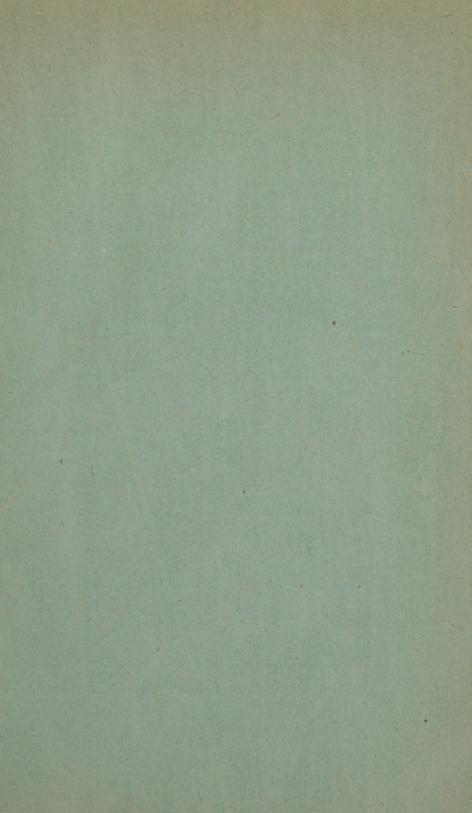
The histological changes in the liver were not so marked or so far advanced as the lesions usually occurring in this organ as the result of the toxines of the bacillus diphtheriæ, but there was a considerable amount of focal necrosis of liver cells, especially about the central veins of the lobules.   There was no leucocytic infiltration of these areas.

It is interesting from the clinical side to note that there were no positive signs of valvular disease.   No murmur was heard; there was absence of cardiac embarrassment, and the pulse was regular and but little accelerated until the last few days of life.

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